A Facile Synthesis of Homologous 4,4'-Dialkanoic Acid Substituted 2,2'-Bipyridines

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Abstract: A convenient three-step synthesis has been developed to prepare a series of homologous 4,4'-dialkanoic acid substituted 2,2'-bipyridines from 4,4'-dimethyl-2,2'-bipyridine.

Key words: bipyridine, carboxylic acid, esterification, ligands, ozonolysis

Functionalized bipyridines have found widespread use as ligands for metals in the areas of bioinorganic chemistry,¹ catalysis,² conducting polymers,³ molecular electronic and optoelectronic devices,⁴ and solar energy conversion.⁵ For the latter application, oligopyridines have been employed as ligands to modulate the photolytic and electronic behavior of metals and to attach these photoactive coordination complexes to the surface of semiconductor films or nanoparticles in photovoltaic models.⁶ As components of such systems, carboxylic acid substituted bipyridines are especially attractive, because of their versatility as precursors for other functional groups and their well-documented interaction with a variety of semiconductors, including TiO₂, ZrO₂, SnO₂, and ZnO.⁷ While most of the published work in this area has employed monosubstituted bipyridines, the incorporation of such ligands in bis- and tris(bipyridine)metal complexes can lead to mixtures of stereoisomers, a difficulty that is circumvented with the synthetic procedure. Therefore, we now report a convenient synthesis of a series of 2,2'-bipyridines functionalized at the 4 and 4' positions with alkanoic acid groups containing one, two, three, four, or five methylene units between the carboxylic moiety and the aromatic ring.

Surprisingly, prior to this work, only two 2,2'-bipyridine-4,4'-diacids were known, 4,4'-Bipyridinedicarboxylic acid is available commercially; and the next higher homolog, 4,4'-bipyridinediethanoic acid, had been obtained in low yield as a side product during the preparation of the corresponding monoacid.⁸ None of the higher members of the series had been synthesized. The synthetic route to the bipyridine diacids 4a–d employs straightforward reactions that are easily accomplished on large scale (Scheme 1). The homologous dialkenes 2a–d were produced by double alkylation of the dianion resulting from deprotonation of the diacids.²⁴ The double bonds in 2a–d were converted to carboxylic acid groups by ozonolysis in basic methanol,¹⁰ followed by hydrolysis of the esters 3a–d with aqueous acid. Basic conditions were also effective in saponifying the esters; however, the direct conversion of the alkenes to the carboxylic acids via an oxidative workup of the ozonolysis was unsuccessful. Another strategy employing dioxolane-protected aldehydes in place of alkenes was thwarted by difficulties in purifying and oxidizing the unmasked aldehydes. Overall, this three-step route provided the diacids 4a–d from 1 in yields between 55 and 61%.

The preparation of a smaller member of this series, 5, also began with 1 (Scheme 2); and it was accomplished by modifying the stoichiometry for the reported synthesis of the monoacid.⁸ Thus, deprotonation with 2.2 equivalents of LDA, followed by the addition of excess dry CO₂, and quenching with dilute aqueous acid afforded 5 in 68% yield.

Scheme 1
In summary, each of the bipyridine diacids 4a–d and 5 has been synthesized in high yield. Current efforts are directed toward the preparation of metal complexes of these ligands, with the ultimate goal of studying their photophysical behavior on semiconductor surfaces.

All reactions were carried out under N\textsubscript{2} unless otherwise stated. THF was freshly distilled from sodium/benzophenone ketyl. All other solvents (analytical grade) and reagents were used without further purification. Anhyd diisopropylamine was purchased from Aldrich. Melting points were recorded on a MelTemp apparatus and are uncorrected. NMR spectra were recorded on a Varian Mercury 400 spectrometer operating at 300 or 75 MHz for 1\textsuperscript{H} or 13\textsuperscript{C}, respectively. Chemical shifts (\delta) are reported in ppm downfield from TMS and are referenced to residual solvent or TMS as the internal standard. IR spectra were recorded with KBr pellets or as liquid film on a Perkin-Elmer 1600 IR spectrometer. UV-Visible spectra were measured on a Cary 50 Bio spectrophotometer. Mass spectra were recorded with a VG70S spectrometer (EI). Column chromatography was performed with Fisher alumina (80–200 mesh). Ozonolyses were conducted with a Welsbach ozonator at 90 V and 3.5–3.8 lbs/inch\textsuperscript{2} pressure. Chromatography of the residue on alumina with 10% EtOAc–hexanes afforded the pure products as pale yellow liquids.

\textbf{Scheme 2}

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UV-Vis (CHCl₃): \( \lambda_{\text{max}} \) (log ε) 243 (4.23), 294 nm (3.18).

1H NMR (CDCl₃, 300 MHz): \( \delta = 8.56 \) (d, \( J = 5.4 \) Hz, 2 H), 8.23 (br s, 2 H), 7.14 (dd, \( J = 5.4, 1.5 \) Hz, 2 H), 3.66 (s, 6 H), 2.74 (t, \( J = 7.5 \) Hz, 4 H), 2.36 (t, \( J = 7.5 \) Hz, 4 H), 2.05 (quint, \( J = 7.5 \) Hz, 4 H).

13C NMR (CDCl₃, 75 MHz): \( \delta = 183.8, 154.7, 154.2, 148.6, 124.5, 121.8, 37.6, 34.6, 29.2, 28.5, 25.7.

MS (FAB): m/z (%) = 385 (16, MH⁺), 313 (44), 160 (100), 154 (25).

FAB HRMS: m/z calcd for \( C_{22}H_{23}N_{2}O_{4} \) (MH⁺) 357.1814, found 357.1828.

2,2'-Bipyridine-4,4'-di(4-butanoic Acid) (4b)
Mp 130–132 °C.

IR (KBr): 3412, 1704, 1685, 1598, 1409, 1176 cm⁻¹.

UV-Vis (H₂O): \( \lambda_{\text{max}} \) (log ε) 202 (3.95), 290 nm (3.53).

1H NMR (D₂O, 300 MHz): \( \delta = 8.53 \) (d, \( J = 5.7 \) Hz, 2 H), 8.09 (br s, 2 H), 7.63 (d, \( J = 5.7 \) Hz, 2 H), 2.77 (t, \( J = 7.5 \) Hz, 4 H), 2.21 (t, \( J = 7.5 \) Hz, 4 H), 1.62 (quint, \( J = 7.8 \) Hz, 4 H), 1.47 (quint, \( J = 7.5 \) Hz, 4 H), 1.22 (quint, \( J = 7.8 \) Hz, 4 H).

13C NMR (D₂O, 75 MHz): \( \delta = 183.8, 154.7, 154.2, 148.6, 124.5, 121.8, 37.6, 34.6, 29.2, 28.5, 25.7.

MS (FAB): m/z (%) = 385 (16, MH⁺), 313 (44), 160 (100), 154 (25).

FAB HRMS: m/z calcd for \( C_{22}H_{23}N_{2}O_{4} \) (MH⁺) 357.1812, found 357.1825.
13C NMR (D2O, 75 MHz): δ = 175.9, 152.2, 145.9, 145.6, 122.2, 120.3, 41.1.

MS (FAB): m/z (%) = 273 (16, MH+), 229 (22), 219 (24), 154 (100).
FAB HRMS: m/z calc for C16H17N2O4 (MH+) 273.0875, found 273.0872.

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References


(2) For example: Collins, J. E.; Fraser, C. L. Macromolecules 1998, 31, 6715.


